This Page Is Inserted by IFW Operations and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.

The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 1 of 23 (Fig. 1A)

SEC	SEQ I D NO:						
9	mouse_E3all	MASEMEPEVQ		AID- RSLLEC SAEEI AGRW	QAT DL NREVY	QHL AHC VP KI	49
4	human_E3αl1	MASELEPEVQ	AI D-RSLLEC	SAEEI AGKWL	QATDLTREVY	QHL AHY VP KI	4
15	mouse_E3αl	MADEEMDGAE	RIMDVSPEPPL	AP QR P AS WWD	QQV DF YT AF L	HHL AQL VPEI	50
7	human_E3αl	MADEEAGGTE	RMEI SAEL PO	TPQRLAS WWD	QQV DF YT AF L	HHL AQL VP E I	50
	Consensus	MA. E	MA. E D L	A W.	Q D	. HLA VP. I	5 (
9	mouse_E3all	YCRGPNPFPQ	KEDTL'AQHI L	L'GP ME WY I CA	EDPALGFPKL	E QANKP SHL C	6
4	human_E3al I	YCRGPNPFPQ	KEDML AQHVL	LGPMEWYLCG	EDPAFGFPKL	E QANKP SHL C	9
15	mouse_E3∝l	YF AE MDP DL E	KQEESVQMSI	LTPLEWLFG	EDPDI CLEKL	KHSG- AFOLC	6
7	human_E3αl	Y F A E MOP DL E	KQEESVQMSI	FTPLEWIFG EDPDI CLEKL	EDPDI CLEKL	KHSG- AFQLC	9
	Consensus	Y P	О	L. P. EWYL. G EDP KL	E DP KL	LC	100
9	mouse_E3αII	GRVFKVGEPT	YSCRDCAVDP	YSCRDCAVDP TCVLCMECFL	GSI HRDHRY:R	MTTSGGGGFC	149
4	human_E3αII	GRVF KVGE PT	YSCRDCAVDP	YSCRDCAVDP TCVLCMECFL	GS1 HRDHRYR	MTTSGGGGFC	149
15	mous e_E3al	GKVFKSGETT	YSCRDCAI DP	TCVLCMDCFQ	SSVHKNHRYK	MHTSTGGGFC	149
7	human_E3αl	GRVFKSGETT	YS CRDCAI DP	TCVLCMDCFQ	DSVHKNHRYK	MHTSTGGGFC	149
	Cons ens us	GRVFK. GE. T	YSCRDCA. DP	TCVLCM CF.	. S. H HRY.	M TS. GGGFC	150
9	mous e_E3aII	DCGDTEAWKE	GPYCQKHKLS	SSEVVEEEDP	L VHL SEDVI A	RTYNI FAI MF	199
4	human_ $E3\alpha II$	DCGDTEAWKE	GPYCQKHELN	TSELEEEEDP	L VHL S E DVI A	RTYNI FAI TF	199
15	mous e_E3al	DCGDTEAWKT	GPFCVDHEPG	RAGTTKESLH	- CPLNEEVI A	QARRI FPSVI	198
7	human_E3αl	DCGDTEAWKT	GPFCVNHEPG	GPFCVNHEPG RAGTI KENSR - CPLNEEVI V	- CPLNEEVI V	QARKI FPSVI	198
	Cons ens us	DCGDT E AWK.	GP. C HE	GP. C HE L. E. VI A I F	L . E . VI A	I F	200

The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 2 of 23 (Fig. 1B)

350	. L. E. PD. EN	. V. V. HS AHQ. F. L. L. SW I . YS R. I . CQ L. E. PD. EN	S.W I YS	AHQ. F. L. L.	. V. V. HS	Consensus	
348	CLREEPDSEN	HVEVLHSEI M AHOKFALRLG SWANKI MSYS SDFROI FCOA CLREEPDSEN	S WANKI MS Y S	AHQKF AL RL G	HVEVLHSEI M	human_E3αl	7
348	CLVEEPGSEN	HVEVLHSVVM AHQKFALRLG SWMINKI MSYS SDFRQI FCQA CLVEEPGSEN	S WANKI MS Y S	AHQKF AL RL G	HVEVLHSVVM	mous e_E3al	15
348	GL QE GP DGE N	KVQVMHSSIV AHQNFGLKLL SWLGSIIGYS DGLRRILCQV GLQEGPDGEN	S W GS I I GYS	AHQNF GL KL L	KVQVMHSSI V	human_E3aII	4
348	GL QE GP DGE N	KVQVMHSSVA AHQNFGLKAL SMLGSVIGYS DGLRRILCQV GLQEGPDGEN	S W GS VI GYS	AHQNF GL KAL	KVQVMHSSVA	mous e_E3aII	9
)))	· · ·					50 5000	
067	HOEINVOUNFL	LUCELAEAUL HIIAI UNEGR KAVNAGAIAA CUEANEUI NO HOEINVOUHPL	KAVNAGATAA	HI I AI UNEGR	LUCELAEAUL	numan_E3&I	7
798	HS EINV S CHP L	COEAKEDI KS HSENVSOHPL	KAVKAGVYA	LUCELAEAUL HIIAI UKEGK KAVKAGVYAI	LUCELAEAUL	mouse_E3al	2
7 70	CECANOVIVA NISACIN- PL		וא ושפוח כח	VINCI CAFAI G FAII VEADGA ASVAIGULOS	אוין עאראן פ	numbn_coan	4
0	1 HO 0 0 H					;	
298	NTSROTK-PL	VNCTQKEAI G FATTVDRDGR RPVRYGDFQY CDQAKTVI VR NTSRQTK-PL	RPVRYGDFQY	FATTVDRDGR	VNCT QKE AI G	mouse_E3aII	9
250	VI Y. LQ. A	. Y. VE WE . E. ELP L EK YYC . LFNDE. H. Y VI Y. LQ. A	EK YYC	. E. ELP L.	. Y. VE WE	Consensus	
248	DHVI YSLQRA	KYVVEMTI WE EEKELPPELQ I REKNERYYC VLFNDEHHSY DHVI YSLQRA	I REKNERYYC	EEKELPPELQ	KYVVE MTI WE	human_E3αl	7
248	DHVI YSL QRA	KYI VEMITI WE EEKELPPELQ I REKNERYYC VLFNDEHHSY DHVI YSLORA	I REKNERYYC	EEKELPPELQ	KYI VEMTI WE	mouse_E3al	15
249	EQVI YTLQKA	KESELPADLE MVEKSDTYYC MLFNDEVHTY EQVIYTLQKA	MVEKSDTYYC	KESELPADLE	RYAVEI LTWE	human_ $E3\alpha II$	4
249	EQVI YTLQKA	RYAVDILTWE KESELPEDLE VAEKSDTYYC MLFNDEVHTY EQVIYTLQKA	VAEKSDTYYC	KESELPEDLE	RYAVDI LTWE	mouse_E3αII	9

Ine Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 3 of 23 (Fig. 1C)

"The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 4 of 23 (Fig. 1D)

Figure 1D

L						
V L	SEQ ID NO:					
9	mouse_E3αII	LKHRDAQGRF QFERYT	OFERYTALOA FKFRRVQSLI		LDLKYVLI SK PTEWSDELRO	498
4	human_E3αII	LRHRDAQGRF QFERYT	QFERYTALQA FKFRRVQSLI	L DL KYVLI SK	LDLKYVLI SK PTEWSDELRQ	498
15	mouse_E3αl	LPEYLDRNN- KFN-FQ	KFN- FQGYSQ DKLGRVYAVI	CDLKYI LI SK PVI WTERLRA	PVI WTERLRA	496
7	human_E3αl	LPEYLDRNN- KFN- FQ	KFN- FQGYSQ DKLGRVYAVI		CDLKYI LI SK PTI WTERLRM	496
	Consensus	L F K RVI	K RV		PT. W LR.	200
9	mouse_E3αII	KFLQGFDAFL ELLKCMQGMD PITRQVGQHI	IQGND PITRQVGQHI	EMEPEWEAAF TLOMKLTHVI	TLOMKLTHVI	548
4	human_E3aII	KFLEGFDAFL ELLKCMQGMD PITRQVGQHI	IQGND PITRQVGQHI	E ME P E WE AA F	TLOMKLTHVI	548
15	mouse_E3αl	QFLEGFRSFL KILTCM	KILTCMOGNE EIRRQVGQHI	EVDPDWEAAI	AI QMQLKNI L	546
7	human_E3αl	OFLEGFRSFL KILTCMOGNE	IQGME EI RRQVGQHI	EVDPDWEAAI	AI QMQLKNI L	546
	Gons ens us	. FLEGF. FL L. CMQGM . I. RQVGQHI	DGM . I . RQVGQHI	E. P. WE AA.	OM L	550
9	mous e_E3aII	S MY QDWCALD EKVLI EAYKK CLAVLT QCHG GFT DGE QPIT LSI CGHS VET	AYKK CLAVLTÖCHK	GFTDGEQPIT	LSI CGHSVET	598
4	human_E3αII	SMMQDWCASD EKVLIEAYKK CLAVLMQCHG GYTDGEOPIT LSICGHSVET	AYKK CLAVLMQCHC	GYTDGEOPIT	LSI CGHSVET	598
15	mouse_E3al	L MF QE WCACD EDLLL VAYKE CHKAV MRCST NF MS STKTV-	AYKE CHKAVMRCST	NF MS STKTV-	VQLCGHSLET	595
7	human_E3al	LIMF QEWCACD EELLLVAYKE CHKAVMRCST SFISSSKTV-	AYKE CHKAVMRCS1	SFISSSKTV-	VQS CGHS LET	595
	Consens us	. M Q. WCA. D E L AYK. C M C F GHS. ET	AYK. CM.C		CGHS. ET	009

"The Human E3α Ubiquitin Ligase Family" Inventors: Han et al. Docket No.: 01017/35966B Sheet 5 of 23 (Fig. 1E)

648 648 645 645 650	698 698 695 700	748 748 738 738
PLSELSPPML PLSELSPPML PFDSFQVEVL SFEDFQVEVL PL	E NF DKDI VML E NF DKDVVML E MY DKDI I ML E MY DKDI I ML E M DKDI I ML	HKDVVQQNNT HKDVVQQNNT DQDL I KQYNT DQDL I KQYNT D Q. NT
I RYCVSQEKV SI HLPI SRLL AGLHVLLSKS EVAYKFPELL PLSELSPPML I YCVSQEKV SI HLPVSRLL AGLHVLLSKS EVAYKFPELL PLSELSPPML KSYKVSEDLV SI HLPLSRTL AGLHVRLSRL GAI SRLHEFV PFDSFQVEVL KSYRVSEDLV SI HLPLSRTL AGLHVRLSRL GAVSRLHEFV SFEDFQVEVL Y. VS V SI HLP. SR. L AGLHV. LS	CAQVHAGMMR RNGFSLVNQI YYYHNVKCRR EMFDKDI VML CAQVHAGMMR RNGFSLVNQI YYYHNVKCRR EMFDKDVVML VAQVVAEMMR RNGLSLI SQV FYYQDVKCRE EMYDKDI I ML VAQVVAEMMR RNGLSLI SQV FYYQDVKCRE EMYDKDI I ML AQV. A. MMR RNG. SL Q YY VKCR. EM DKDI . ML	QTGVS MWDPN HFLMI MLSRF ELYQLFSTPD YGKRFSSEVT HKDVVQQNNT QTGVS MWDPN HFLMI MLSRF ELYQI FSTPD YGKRFSSEIT HKDVVQQNNT QI GASI MDPN KFLLLVLQRY ELTDA FNKTI STK DQDLI KQYNT QI GASLMDPN KFLLLVLQRY ELAEA FNKTI STK DQDLI KQYNT QI GASLMDPN KFLLLVLQRY ELAEA FNKTI STK DQDLI KQYNT QI GS. MDPN FLL.R. ELTK.SDQ. NT
AGLHVLLSKS AGLHVLLSKS B AGLHVRLSRL AGLHVRLSRL AGLHV.LS	CAQVHAGMMR RNGFSLVNQI CAQVHAGMMR RNGFSLVNQI VAQVVAEMMR RNGLSLI SQV VAQVVAEMMR RNGLSLI SQV . AQV. A. MMR RNG. SL Q.	ELYQLFSTPD ELYQI FSTPD ELTDA ELAEA
SI HLPI SRLL II HLPVSRLL SI HLPLSRTL SI HLPLSRTL SI HLPLSRTL	CAQVHAGMMR RNGFSLVNQI CAQVHAGMMR RNGFSLVNQI VAQVVAEMMR RNGLSLI SQV VAQVVAEMMR RNGLSLI SQV . AQV. A. MMR RNG. SL Q.	HFLM MLSRF HFLM MLSRF KFLLLVLQRY KFLLLVLQRY
I RYCVS QE KV I YCVS QE KV KS YKVS E DL V KS YRVS E DL V Y . VS V	I EHPLRCLVL I EHPLRCLVL VEYPLRCLVL VEYPLRCLVL	OT GVS MWDP N OT GVS MWDP N OI GAS I MDP N OI GAS I MDP N O G S MDP N
mous e_E3αII huma n_E3αII mous e_E3αI huma n_E3αI Cons ens us	mous e_E3αII huma n_E3αII mous e_E3αI huma n_E 3αI Cons ens us	mous e_E3αII huma n_E3αII mous e_E3αI huma n_E3αI
6 1 2 2	6 4 4 2 2	6 4 1 2

"The Human E3α Ubiquitin Ligase Family" Inventors: Han et al. Docket No.: 01017/35966B Sheet 6 of 23 (Fig. 1F)

Figure 1F

9006	I NL L NCD! MM VN. L. CDVM	SKTOMSKAEH MOKKRRKOEN KDEALPPPP PEFCPAFSKV INLLNCDIMM SSKAE O.KO D. ALPPP P. FCP. F VN. L. CDVM	SKTOHSKAEH MOKKRRKOEN KDEALPPPPP PEFCPAFSKV SSKAE Q.K Q D. ALPPP P. FCP. F	MOKKRKKOEN O.KO.	SKTQHSKAEH SSKAE.	human_E3αl Consensus
888	VNLLSCDVM	PEFCPAFSKV V	KTQHSKAEH MQKKRRKQEN KDEALPPPPP PEFCPAFSKV	MOKKRRKQEN	S K T QHS K A E H	mouse_E3al
868	VNI LQS DVML		EDTALPPPVL	AQRKL KRQNR	SRAEQSKAEE AQRKLKRQNR EDTALPPVL	human_E3αII
868	VNI L QCDVML	PPFCPLFASL \		AQRKLKRENK	SRAEQSKAEE AQRKLKRENK EDTALPPPAL	mo us e_E3αII
850	K. FN. YFYH.	. LPE. EN. ET G. E. VI VA . FKKPG G. G. YELK. E	N. FKKPG G.	G. E. VI VA	. LPE. EN. ET	Cons ens us
838	K DF NMY F Y HY	NLPENENNET GLENVINKVA TFKKPGVSGH GVYELKDESL KDFNMYFYHY	\ TFKKPGVSGH	GLE NVI NKVA	NL P E NE NNET	human_E3αl
838	KDF NMY F Y HY	GLENVI NKVA TFKKPGVSGH GVYELKDESL KDFNMYFYHY	TFKKPGVSGH		NL PENENNET	mous e_E3al
848	KEFNLYFYHF	GNESVIEAVA HFKKPGLTGR GMYELKPECA KEFNLYFYHF	N HFKKPGLTGR		SLPEDENKET	$human_E3\alpha II$
848	KEFNLYFYHF	SLPEDENKET GMESVIESVA HFKKPGLTGR GMYELKPECA KEFNLYFYHF	N HFKKPGLTGR	GMESVI ESVA	SLPEDENKET	mous e_E3aII
800	. PM HSK	. REI I H. L. I	VGER PG VG. VI	VGERPG	LI EEMLI	Consensus
788	EP MP HS AI AK	MREI I HLLCI	YI VGERYVPG VGNVTKEEVT	YI VGERYVPG	LI EEMLQVLI	human_E3αl
788	EPMPHSAI AR	MREI.THL LCI	YI VGERYVPG VGNVTREEVI	YI VGERYVPG	LI EEMLQVLI	mouse_E3∝l
798	KP MAHS EL V K	KREI I HQLSI	MLVGERFSPG VGQVNATDEL		LI EEMLYL!!	$humen_E3\alpha II$
798	KP MAHS EL V K	KREI I HQLSI	LI EEMLYLII MLVGERFNPG VGQVAATDEI	MLVGERFNPG	LI EEMLYLI I	mouse_E3aII

"The Human E3α Ubiquitin Ligase Family" Inventors: Han et al. Docket No.: 01017/35966B Sheet 7 of 23 (Fig. 1G)

Figure 1G

	m	æ		7	C	m	m		₹	C	S	S		₹†	
	948	948	937	937	950	966	966	987	984	1000	104	104	1037	103,	105
	GMAL QEEKHH LENAVEGHVQ	GMAL QEEKQH LENVTEEHVV	ALGLLEEKQQ LQKAPEEEV-	ALGLLEEKQQ LQKAPEEEV-	L. EEKQ. L A. EE. V.	FTFTQKISK PGDAPHNSPS ILAMLETLQN APSLEAHKDM IRWLLKMFNA	FTFTOKISK PGEAPKNSPS ILAMLETLON APYLEVHKDM IRW LKTFNA	I TW LOWFDT	I I TW LONFDT	II. WIL. MF	DKAERKRKAE I ARLRREKI M 1046	I ARL RREKI M 1046	AARLHRQKI M 1037	VKRLREKSCL I VATTSGSES I KNDEI THDK EKAERKRKAE AARLHRQKI M 1034	VK. RE. CEEE DK . KAERKRKAE . ARL. R. KI M 1050
	GMAL QE E KHH	GMAL QE E KOH	ALGLLEEKQQ	ALGLLEEKQQ		APSLEAHKDM	APYLEVHKDM	I PQLEGQKDM	I PQLEGQKDM	. P. LE.: KDM		DKAERKRKAE	EKAERKRKĀE	EKAERKRKAE	. KAERKRKAE
	S ML QRVL HLI	S ML QRVL HLI	GML QMAFHI L	GML QMAFHI L	. MLQ H	ILAMLETLON	ILAMLETLON	IOMLLERLKG	LLEKLKG	ILE.L	TI MEESSRDK	PTSPVAETEG TI MEESSRDK	I KSEEI THDK	I KNDEI THDK	EE DK
	MGTILQWA VEHHGSAWSE SMLQRVLHLI	VEHNGY AWSE SMLQRVLHLI	LRTIFERA VDTESNLWTE GMLQMAFHIL	LRTVFERA I DTDS NLWTE GMLQMAFHI L	I TI A V W. E . MLQ H	P GDAP HNS P S	PGEAPKNSPS	DFYHKASR LGSSAMNAQN I QMLLERLKG I PQLEGQKDM I TW LQMFDT	FDFYHKASR LGSSAMNIQM LLEKLKG IPQLEGQKDM ITW LQMFDT	F. F K. S G N I LE. L P. LE KDM I . M L. MF	KKIRECS SSSPVAEAEG TI MEESSRDK	PTSPVAETEG	VKRLREKSCL VVATTSGLEC I KSEEI THDK	I VATTSGSES	ш.
	YI MGTI LQWA	CI MGTI LOWA	YI LRTI FERA		YI TI A	TFTFTQKI SK	TFTFTQKI SK	AF DF Y HKAS R	TFDFYHKASR	TF. F K. S.	I KKI RECS	VKKMRESS	VKRLREKSCL	VKRLREKSCL	VK. RE. C.
SEQ I D NO:	mouse_E3aII	human_E3αII	mouse_E3αl	human_E3αl	Cons ens us	mous e_E3aII	human_E3αII	mouse_E3αl	human_E3αl	Cons ens us	mouse_E3aII	human_E3a1	mouse_E3αl	human_E3αl	Consensus
SEQ	9	4	15	7		9	4	15	7		9	4	15	7	

"The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 8 of 23 (Fig. 1H)

1094	1094	1087	1084	1100	1144	1144	1137	1134	1150	,	1193	1193	1184	1181	1200
AQMSEMQRHF IDENKELFQQ TLELDTSASA TLDSSPPV SDAALTALGP 1094	I DENKELFQQ TLELDASTSA VLDHSPVA SDMTLTALGP 1094	AQMSALQKNF IETHKLMYDN TSEVTGKEDS IMEEESTSAV SEASRIALGP 1087	I ETHKLMYDN TSEMPGKEDS I MEEESTPAV SDYSRI ALGP 1084	IK T.E S.P.V SDALGP 1100	AQTQVPEPRQ FVTCI LCQEE QEVTVGSRAM VLAAFVQRST VLSKDRTKTI 1144						AD-PEKYDPL FMHPDLSCGT HTGSCGHVMH AHCWQRYFDS VQAKEQRRQQ 1193	HTSSCGHI MH AHCWQRYFDS VQAKEQRRQQ 1193	YTGSCGHVMH AVCWQKYFEA VQLSSQQ 1184	ELSGEALDPL FMDPDLAYGT YTGSCGHVMH AVCWQKYFEA VQLSSQQ 1181	E DPL FM PDL GT .TGSCGHVMH A. CWQ. YF VQQQ 1200
TLDSSPPV	VL DHS PVA	I MEEESTSAV	INEEESTPAV	S. P. V	VLAAFVQRST	VLAAFVQRST	VLSACVQKST	VLSACVQKST	VL. A. VQ. ST		AHCWQRYF DS	AHCWQRYFDS	AVCWOKYFEA	AVCWQKYFEA	A. CWQ. YF
TLELDTSASA	TLELDASTSA	TSEVTGKEDS	TSEMPGKEDS	T. E	QEVTVGSRAM	QEVKVESRAM	QEVKLENNAM	QEVKI ENNAM	QEVK. E AM	. :	HT GS CGHV MH	HTSSCGHI MH	YTGSCGHVMH	YT GS CGHVMH	. TGSCGHVMH
I DENKELFQQ	I DE NKELFQQ	I ET HKL MY DN	I ETHKL MYDN		FVTCI LCQEE	TQTQVPEQRQ FVTCI LCQEE QEVKVESRAM VLAAFVQRST VLSKNRSKFI	KRGPAVTEKE VLTCI LCQEE QEVKLENNAM VLSACVQKST ALTQHRGKPV	KRGPSVTEKE VLTCI LCQEE QEVKI ENNAM VLSACVQKST ALTQHRGKPI			F MHP DL S CGT	F MHP DL S CGT	F MDP DL AHGT	F MDP DL AYGT	FM PDLGT
AQMS E MQR HF	A QWS E MORHF	AQMS AL QKNF	AQMS AL QK NF	AQMSQF	AQTQVPEPRQ	TQTQVPEQRQ	KRGPAVTEKE	KRGPSVTEKE	•		AD-PEKYDPL	QD- PEKYDPL	DHL GETL DPL	ELSGEALDPL	E DPL
mouse_E3aII	human_ $E3\alpha II$	mouse_E3al	human_E3αl	Consensus	mouse_E3aII	human_E3αII	mouse_E3αl	human_E3 α	Consensus		mo us e_E 3α II	human_E3αII	mouse_E3al	human_E3αl	Consens us
9	4	15	7		9	4	15	7			9	4	15	7	

"The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 9 of 23 (Fig. 1I)

1350	W. TCA. TI	YS. S I KEM F. T Y GLKV. P. E. DPRVP W. TCA. TI	Y GLKV.	I KEM F. T	YS. S	Consensus	
1329	LTWSTCAFT!	JESSIKYSNS I KEMJILFAT TIYRI GLKVP PDERDPRVPM LTWSTCAFTI	TI YRI GLKVP	I KEMVI LFAT	VESSI KYSNS	human_E3αl	7
1333	MT W5 T CAFT!	VQSSVKYSNS I KEMVI LFAT TI YRI GLKVP PDELDPRVPM MTWSTCAFTI	TI YRI GLKVP	I KEMVI LFAT	VQS S V K Y S NS	mouse_E3al	15
1340	MCWGS CAYT!	PNEEDPRVPI	ATYKVGLKVH	RPKI PYSES I KEMLTTFGT ATYKVGLKVH PNEEDPRVPI	FRPKI PYSES	human_E3αII	4
1340	LCWGTCAYTI	PNEGDPRVPI	AAYKVGLKVH	FYPRNPYSDS I KEMLTTFGT AAYKVGLKVH PNEGDPRVPI	FYPRNPYSDS	mouse_E3aII	9
1300		K P	. K P	:	. L.A. WI . TV.	Consensus	
1279	LEFHSI LSFG	TLARW QTVL ARISGYNIRH AKGENP-IPI FFNQGMGDST LEFHSILSFG 1279	AKGENP-1P1	ARI SGYNI RH	TLARW QTVL	human_E3αl	7
1283	FEFHSILSFG 1283	L F NQGMGDS T	AKGEAPAVPV	ARI SGYNI KH AKGEAPAVPV LFNQGMGDST	TLARW QTVL	mouse_E3αl	15
1290	LOLPEGFRPD 1290	STKNSENVDE	QQI KALQFLR KEESTP-NNA STKNSENVDE	QQI KALQFLR	NLTQW RTIS	human_E3αII	4
1290	I PI PEGFRPD 1290		RKHNAA- DTS	DLAQWIRAVI QQIKVVQMLR RKHNAA-DTS SSEDTEAMNI	DL AQWI RAVT	mous e_E3αII	9
1250		E. GE. LCPLC L. NTVI P L. P I . S	L. NTVI P.	E. GE. LCPLC	R D.	Cons ens us	
1230	ENADAL AQL L	I PLQPQKI NS ENADALAQLL	ESGEYLCPLC KSLCNTVIPI		RI HVDL - FDL	human_E3αl	7
1233	E NAE AL AQL L	I PLQPQKI NS ENAEALAQLL	KSLCNTVI PI	ESGEYLCPLC KSLCNTVI PI	RI HVDL - FDL	mouse_E3αl	15
1241	NRLN- FSDQP	L-LPPRNI FN NRLN- FSDQP 1241	ECLSNTVIPL	RLRLHTSYDV ENGEFLCPLC ECLSNTVI PL	RLRLHTSYDV	human_E3αII	4
1241	RRLN- FSDQP	RLRLHTSYDV ENGEFLCPLC ECLSNTVIPL L-LPPRSILS RRLN-FSDQP 1241	ECLSNTVIPL	ENGEFLCPLC	RLRLHTSYDV	mouse_ $E3\alpha II$	9

"The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 10 of 23 (Fig. 1J)

SEQ ID NO:

1390 1390 1383 1379 1400	1437 1437 1433 1429 1450	1482 1482 1483 1475 1500
LLPVVQGHFC SVSVVQGHFC PQVLIHKHLA PQVLIQKHLV	DFSGSSL 1437 DFSGISL 1437 DTVDLQPSPL 1433 DPVDLQPSSV 1429 DSSL 1450	TGEEELAILS 1482 PCEESAVLA 1482 DSEEARCASA 1483 DSEEAHSASS 1475 EE 1500
RFAAAHWTVA RFAAAHWTVA QFAVAQRATC QFAVAQRITC FA.A	VLAFPALQCQ VLAFPALQCQ VLAFPSLYWD VLAFPSLYWD	GMDQENP GMDQENP PGPPLAEGEE PLAQVQE
RLDDCLRSLT RLDDCLRSLT RQHSGLKALM RQHNGLKALM RLL.	IDMFHLLVGL IDMFHLLVGL VDLFHVLVGA IDLFHVLVGA ID. FH. LVG .	ILLTSCTEEN ILLTSCTEEN ILLTTDTDLS ILLTVDTGL-
QSIERILSDE EKPVFGPLPC RLDDCLRSLT QSIERILSDE DKPLFGPLPC RLDDCLRSLT QAIENLLGDE GKPLFGALQN RQHSGLKALM QAIENLLGDE GKPLFGALQN RQHNGLKALM Q.IEL.DE .KPLFG.L RLL.	SYEDLPCILD SHEELPCILD QSENTPGLLS KSEDTPCLLS	HLVTMAHIVQ ILLTSCTEEN HLVTMAHIIQ ILLTSCTEEN HLITMAHMLQ ILLTTDTDLS HLITMAHMLQ ILLTVDTGL- HL.TMAHQ ILLTT
QSIERILSDE QSIERILSDE QAIENLLGDE QAIENLLGDE Q.IEL.DE	KLFASLVPSD KLFASLVPND RLLSVILPNL RLLSVVLPNI	ATGDLHIF GTGDLHIF SSSYNHLYLF SSSYNHLYLF
6 mouse_E3αII 4 human_E3αII 15 mouse_E3αI 2 human_E3αI Consensus	6 mouse_E3αII 4 human_E3αII 15 mouse_E3αI 2 human_E3αI Consensus	6 mouse_E3aII 4 human_E3aII 15 mouse_E3aI 2 human_E3aI

"The Human E3α Ubiquitin Ligase Family" Inventors: Han et al. Docket No.: 01017/35966B Sheet 11 of 23 (Fig. 1K)

Figure 1K

"The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 12 of 23 (Fig. 1L)

		1774		I FELL O E. NO. L. G. WO. L	. I . EEI 0	Consensus	
		1749		CITEELARSQ ETNOMLFGFN WOLL	CI I EEI ARSQ	human_E3αl	7
		1757		CIIEEIARSQ ETNOMLFGFN WOLL	CI I EEI ARSQ	mouse_E3αl	15
		1755		SVTEEI GHAQ EANQTLVGI D WOHL	SVTEE! GHAQ	human_E3aII	4
		1755		SI TEEI GHAQ EANQTLVGI D WQHL	SI TEEI GHAQ	muse_E3aII	9
1750	GK GC . Y PYLD. Y GETD. GL. RG NPLHL ER. RK WQQH 1750	NPLHLER.	GETD. GL. RG	. Y PYLD. Y	GK GC	Consensus	
1725	VLVEGKARGC AYPAPYLDEY GETDPGLKRG NPLHLSRERY RKLHLVWQQH 1725	NPLHLSRERY	GET DPGL KRG	AYPAPYL DEY	VLVEGKARGC	human_E3αl	. 2
1733	VLVEGKARGC AYPAPYLDEY GETDPGLKRG NPLHLSRERY RKLHLVWQQH 1733	NPL HL SRERY	GET DP GL KRG	AYPAPYLDEY	VLVEGKARGC	mouse_E3al	15
1731	LFLAGKTKGC FYSPPYLDDY GETDQGLRRG NPLHLCKERF KKI QKLWHQH 1731	NPL HL CKERF	GETDQGLRRG	FYSPPYLDDY	LFLAGKTKGC	human_E3αII	4
1731	LFLAGKTKGC FYSPPYLDDY GETDQGLRRG NPLHLCQERF RKI QKLWQQH 1731	NPL HL CQERF	GETDQGLRRG	FYSPPYLDDY	LFLAGKTKGC	mouse_E3aII	9
1700	LCL. CG LC SQ CCQ GE. VGAC H CG. GV. 1 FL REC. V 1700	H CG. GV.	. GE. VGAC	SQ CCQ	LCL. CG LC	Cons ens us	
1675	LCLFCGAILC SQNI CCQEIV NGEEVGACIF HALHCGAGVC IFLKI RECRV 1675	HAL HCGAGVC	NGEEVGACI F	S QNI CCQEI V	LCLFCGAI LC	human_E3αl	7
1683	LCLFCGAILC SQNI CCQEIV NGEEVGACVF HALHCGAGVC I FLKI RECRV 1683	HAL HCGAGVC	NGEEVGACVF	S QNI CCQEI V	LCLFCGAI LC	mouse_E3al	15
1681	LCLVCGSLLC SQSYCCQTEL EGEDVGACTA HTYSCGSGVG I FLRVRECQV 1681	HTYSCGSGVG	EGEDVGACTA	SQSYCCQTEL	LCLVCGSLLC	human_ $E3\alpha II$	4
1681	LCLVCGSLLC SQSYCCQAEL EGEDVGACTA HTYSCGSGAG IFLRVRECQV 1681	HTYS CGS GAG	EGEDVGACTA	SQSYCCQAEL	LCL VCGS LLC	mous e_E3αII	9

"The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 13 of 23 (Fig. 2)

FIG. 2

Tth Expression Profile of huE3 α -II in Human Tissues

Brain	Heart	Skeletal muscle	Colon	Thymus	Spleen	Kidney	Liver	Small intestine	Placenta	Lung	Leukocyte
$\mathbf{\Theta}$	I	S	\circ	-	S	\mathbf{X}		S	Δ.	二	ت

137

9.5kb ---

7.5kb —

4.4kb —

2.4kb —

"The Human E3a Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 14 of 23 (Fig. 3)

FIG. 3

Tth Expression Profile of huE3 α -l in Human Tissues

Heart Brain Placenta Lung Liver Skeletal Muscle Kidney

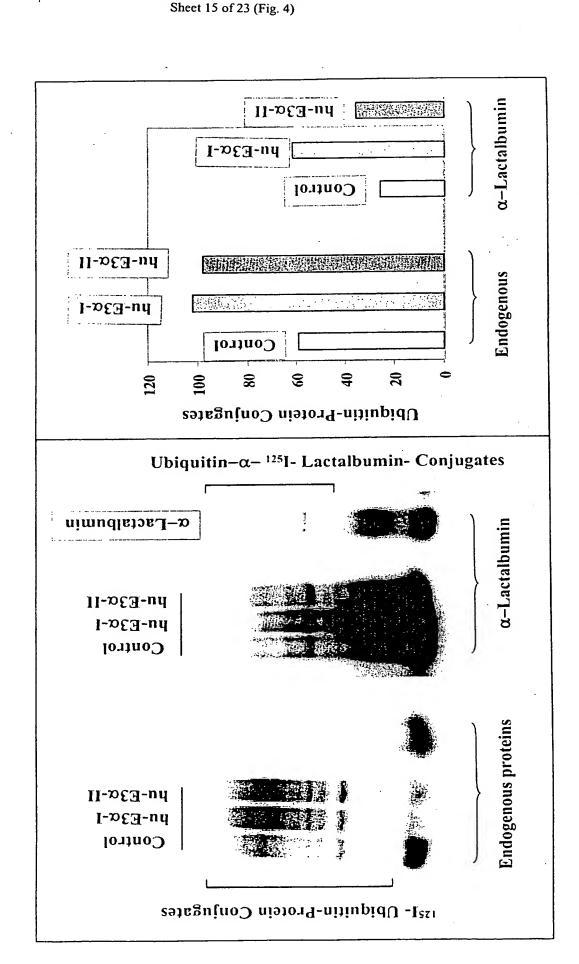
9.5kb __ 7.5kb __

4.4kb -

2.4kb -

The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B

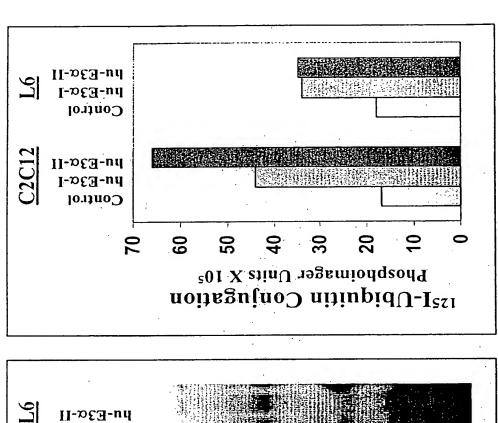
Figure 4
Ubiquitination of Endogenous Proteins

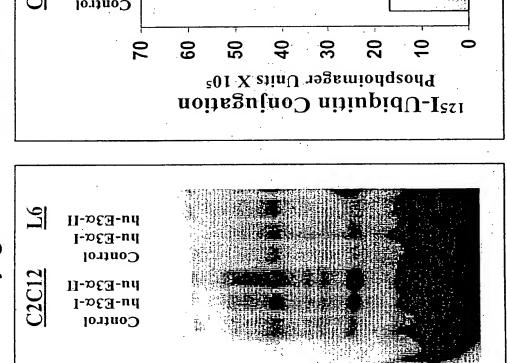


"The Human E3a Ubiquitin Ligase Family" Inventors: Han et al.

Docket No.: 01017/35966B Sheet 16 of 23 (Fig. 5)

Transfection of Human E3a-I or E3a-II cDNA Stimulates Ubiquitin Conjugation in Cultured Muscle Cell Lines Figure 5





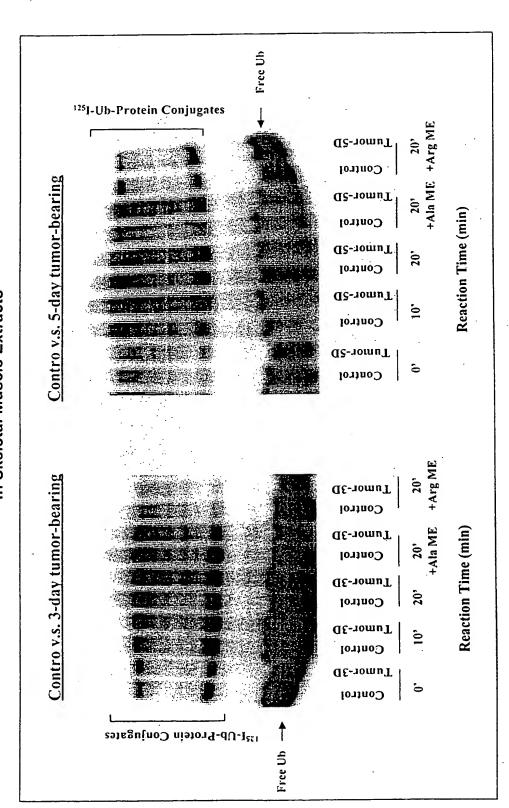
Conjugates

1251-Ubiquitin-Protein

"The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 17 of 23 (Fig. 6)

Figure 6

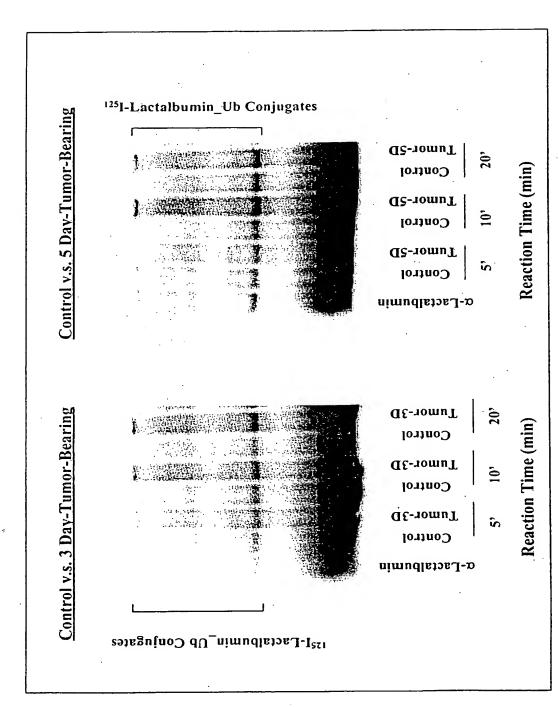
 $^{125}\mbox{I-Ubiquitin}$ Conjugation to Muscle Proteins and Its Sensitivity to E3 α Inhibitor in Skeletal Muscle Extracts



"The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 18 of 23 (Fig. 7)

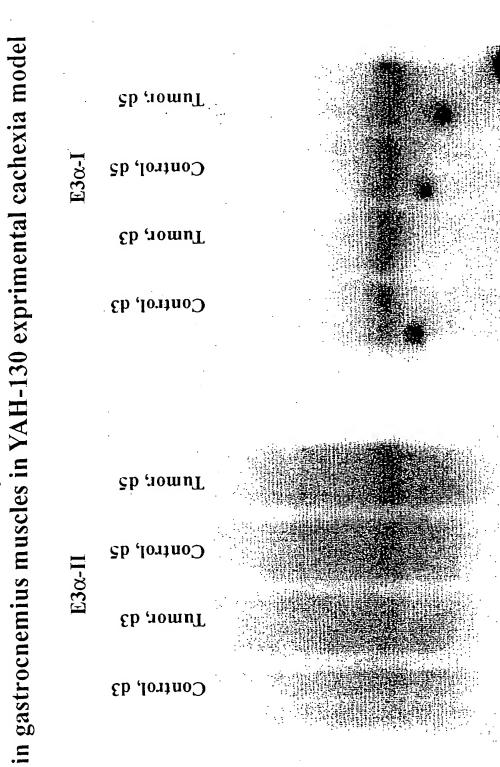
Figure 7

Rates of Ubiquitination of N-end Rule Substrate α-Lactalbumin in Skeletal Muscle Extracts



The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 19 of 23 (Fig. 8)

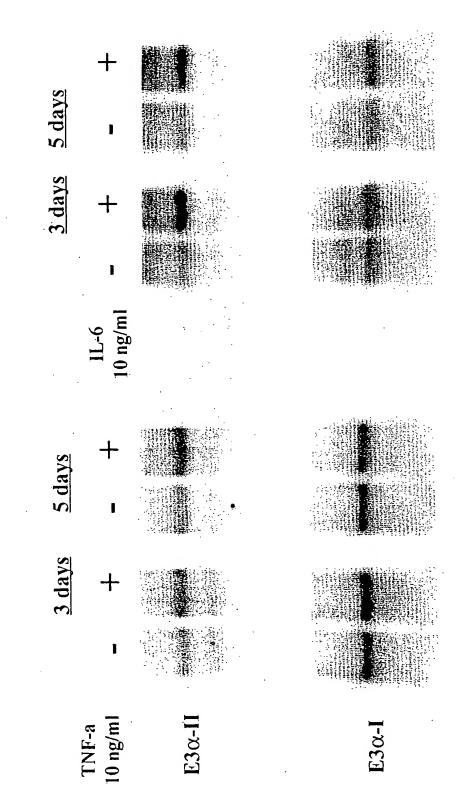
Northern blot analysis of E3 α -I & E3 α -II expression Figure 8



Հ<u>լ</u>թ 'ւօաոյ 71b ,b91 insq Northern blot analysis of E3 α -I and E3 α -II expression in control, d17 gastrocnemius muscle and cardiac muscle tumor, dll in C26 experimental cachexia model pari fed, d12 control, d12 71b nomui 71b ,bal insq control, d17 tumor, dl2 pari fed, d12 control, dl2 Gastroenmius

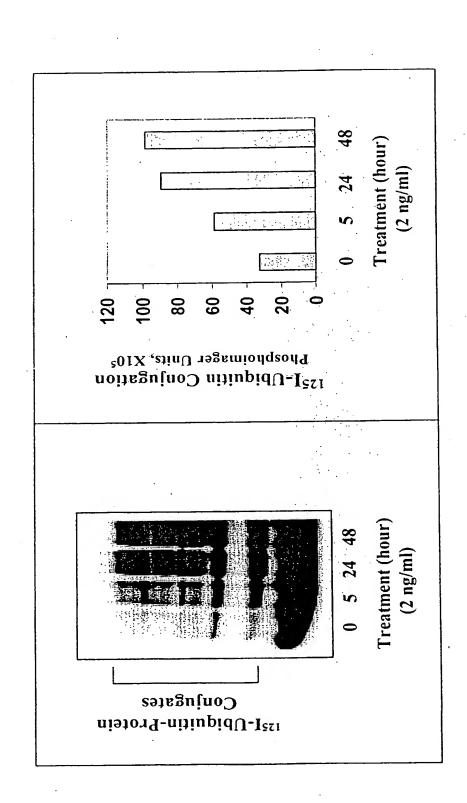
The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 21 of 23 (Fig. 10)

induce E3α-II Expression in C2C12 myostube culture Proinflammatory cytokines TNF- α and IL-6 Figure 10



"The Human E3α Ubiquitin Ligase Family"
Inventors: Han et al.
Docket No.: 01017/35966B
Sheet 22 of 23 (Fig. 11)

IL-6 Elicits Accelerated Ubiquitination in C2C12 Myotube Cultures



Inventors: Han et al.

Docket No.: 01017/35966B

Sheet 23 of 23 (Fig. 12)

 TNF_{α} Elicits Accelerated Ubiquitination in C2C12 Myotube Cultures

